

We claim:

1. A method of eliciting an immune response against an EphA2-expressing cell, said method comprising administering to an individual a composition comprising an EphA2 antigenic peptide in an amount effective to elicit an immune response against an EphA2-expressing cell.

5 2. The method of claim 1, wherein the EphA2 antigenic peptide is not TLADFDPRV (SEQ ID NO:3); VLLLVLAGV (SEQ ID NO:4); VLAGVGFFI (SEQ ID NO:5); IMNDMPIYM (SEQ ID NO:6); SLLGLKDQV (SEQ ID NO:7); WLVPIGQCL (SEQ ID NO:8); LLWGICALAA (SEQ ID NO:9); GLTRTSVTV (SEQ ID NO:10); NLYYAESDL (SEQ ID NO:11); KLNVEERSV (SEQ ID NO:12); IMGQFSHHN (SEQ ID NO:13); YSVCNVMSG (SEQ ID NO:14); MQNIMNDMP (SEQ ID NO:15); EAGIMGQFSHHNIIR (SEQ ID NO:16); PIYMYSVCNVMSG (SEQ ID NO:17); or DLMQNIMNDMPIYMY (SEQ ID NO:18).

10 3. The method of claim 1, wherein the composition further comprises an adjuvant.

15 4. The method of claim 1, wherein the composition comprises a heat shock protein bound to said EphA2 antigenic peptide.

20 5. The method of claim 1, where the polypeptide further comprises a protein transduction domain.

25 6. The method of claim 5, wherein the protein transduction domain is the Antennapedia or the HIV tat protein transduction domain.

7. A method of eliciting an immune response against an EphA2-expressing cell, said method comprising administering to an individual a composition comprising an EphA2 antigenic peptide expression vehicle in an amount effective to elicit an immune response against an EphA2-expressing cell.

25 8. The method of claim 7, wherein the expression vehicle is a nucleic acid encoding said EphA2 antigenic peptide operably linked to a promoter.

9. The method of claim 8, wherein the nucleic acid is DNA.

10. The method of claim 9, wherein the DNA is conjugated to a carrier.

11. The method of claim 8, wherein the carrier is asialoglycoprotein.

12. The method of claim 8, wherein the carrier is transferrin.

5 13. The method of claim 8, wherein the carrier is polymeric IgA.

14. The method of claim 7, wherein the expression vehicle is an infectious agent comprising a nucleic acid, said nucleic acid comprising a nucleotide sequence encoding said EphA2 antigenic peptide operably linked to a promoter.

10 15. The method of claim 14, wherein the sequence encoding said EphA2 antigenic peptide is codon-optimized for expression in said infectious agent.

16. The method of claim 14, wherein the infectious agent is coated with a reagent that targets the infectious agent to EphA2-expressing cells.

17. The method of claim 16, wherein the reagent is an anti-EphA2 antibody.

15 18. The method of claim 14, wherein the infectious agent is coated with a reagent that targets the infectious agent to antigen-presenting cells.

19. The method of claim 14, wherein the infectious agent is a bacterium.

20. The method of claim 19, wherein the bacterium is attenuated.

21. The method of claim 19, wherein the nucleic acid comprises a nucleotide sequence encoding a secretory signal operatively linked to the sequence encoding the EphA2 antigenic peptide.

20 22. The method of claim 21, wherein the secretory signal is a SecA secretory signal.

23. The method of claim 19, wherein the bacterium is *Pseudomonas aeruginosa*.
24. The method of claim 19, wherein the bacterium is not *Listeria*.
25. The method of claim 14, wherein the infectious agent is a virus.
26. The method of claim 25, wherein the virus is a retrovirus.
- 5 27. The method of claim 26, wherein the retrovirus is a lentivirus.
28. The method of claim 25, wherein the virus is an adenovirus.
29. The method of claim 25, wherein the virus is an adeno-associated virus.
30. The method of claim 25, wherein the virus is herpes simplex virus.
31. The method of claim 25, wherein the virus is attenuated.
- 10 32. The method of claim 7, wherein the expression vehicle is a mammalian cell comprising a recombinant nucleic acid, said nucleic acid comprising a nucleotide sequence encoding said EphA2 antigenic peptide.
33. The method of claim 32, wherein the mammalian cell is a human cell.
- 15 34. The method of claim 32, wherein the mammalian cell is encapsulated within a membrane.
35. The method of claim 34, wherein said administering is by means of implantation.
36. A method of eliciting an immune response against an EphA2-expressing cell, said method comprising administering to an individual a composition comprising antigen presenting cells sensitized with an EphA2 antigenic peptide.
- 20 37. The method of claim 36, further comprising prior to said administration the step of sensitizing the antigen presenting cells.

38. The method of claim 37, wherein the antigen presenting cells are sensitized by a method comprising: contacting the cells with a composition comprising one or more EphA2 antigenic peptides in an amount effective to sensitize the cells.

39. The method of claim 36, wherein the composition further comprises a heat shock
5 protein.

40. The method of claim 39, wherein the heat shock protein is hsp70, gp96, or hsp90.

41. The method of claim 36, wherein the antigen presenting cells are autologous to the individual.

42. The method of claim 36, wherein the antigen presenting cells are non-autologous to the
10 individual.

43. The method of claim 36, wherein the antigen presenting cells are macrophages.

44. The method of claim 36, wherein the antigen presenting cells are dendritic cells.

45. The method of claim 1, 7, or 36, wherein the individual has cancer.

46. The method of claim 45, wherein said cancer is of an epithelial cell origin or
15 endothelial cell origin.

47. The method of claim 45, wherein said cancer comprises cells that overexpress EphA2 relative to non-cancer cells having the tissue type of said cancer cells.

48. The method of claim 45, wherein said cancer is a cancer of the skin, lung, colon, ovary, esophagus, breast, prostate, bladder or pancreas or is a renal cell carcinoma or melanoma.

20 49. The method of claim 1, 7, 36, or 52, wherein the individual has a non-neoplastic hyperproliferative disorder.

50. The method of claim 49, wherein the hyperproliferative disorder is an epithelial cell disorder.

51. The method of claim 50, wherein the hyperproliferative is asthma, chronic pulmonary obstructive disease, lung fibrosis, bronchial hyper responsiveness, psoriasis, and seborrheic dermatitis.

52. A method of eliciting an immune response against an EphA2-expressing cell, said method comprising administering to an individual a composition comprising an anti-idiotypic antibody or antigen-binding fragment thereof which immunospecifically binds to an idioype of an anti-EphA2 antibody in an amount effective to elicit an immune response against an EphA2-expressing cell.

10 53. A method of treating a human individual having a hyperproliferative disorder of EphA2-expressing cells, said method comprising administering to the individual a composition comprising an EphA2 antigenic peptide in an amount effective to treat a hyperproliferative disorder of EphA2-expressing cells.

15 54. A method of treating a human individual having a hyperproliferative disorder of EphA2-expressing cells, said method comprising administering to the individual a composition comprising an EphA2 expression vehicle in an amount effective to treat a hyperproliferative disorder of EphA2-expressing cells.

20 55. A method of treating a human individual having a hyperproliferative disorder of EphA2-expressing cells, said method comprising administering to the individual a composition comprising antigen presenting cells sensitized with an EphA2 antigenic peptide in an amount effective to treat a hyperproliferative disorder of EphA2-expressing cells.

25 56. A method of treating a human individual having a hyperproliferative disorder of EphA2-expressing cells, said method comprising administering to an individual a composition comprising an anti-idiotypic antibody or antigen-binding fragment thereof which immunospecifically binds to an idioype of an anti-EphA2 antibody in an amount effective to elicit treat a hyperproliferative disorder of EphA2-expressing cells.

57. The method of claim 53, 54, 55, or 56, wherein the individual has cancer.

58. The method of claim 57, wherein said cancer is of an epithelial cell origin.
59. The method of claim 57, wherein said cancer comprises cells that overexpress EphA2 relative to non-cancer cells having the tissue type of said cancer cells.
60. The method of claim 57, wherein said cancer is a cancer of the skin, lung, colon, breast,
5 prostate, bladder or pancreas or is a renal cell carcinoma or melanoma.
61. The method of claim 53, 54, 55, or 56, wherein the individual has a non-neoplastic hyperproliferative disorder.
62. The method of claim 61, wherein the hyperproliferative disorder is an epithelial cell disorder.
- 10 63. The method of claim 62, wherein the hyperproliferative disorder is asthma, chronic pulmonary obstructive disease, lung fibrosis, bronchial hyper responsiveness, psoriasis, and seborrheic dermatitis.
64. The method of any one of claims 1, 7, 36, 53, 54, and 55, wherein the EphA2 polypeptide comprises full length EphA2.
- 15 65. The method of any one of claims 1, 7, 36, 53, 54, and 55, wherein the EphA2 polypeptide comprises the extracellular domain or intracellular domain of EphA2.
66. The method of any one of claims 1, 7, 36, 53, 54, and 55, wherein the EphA2 polypeptide comprises the intracellular domain and extracellular domain of EphA2 and lacks the transmembrane domain.
- 20 67. The method of claim 66, wherein the EphA2 polypeptide lacks tyrosine kinase activity.
68. The method of claim 67, wherein the EphA2 polypeptide lacks tyrosine kinase activity due to a lysine to methionine substitution at position 646 of EphA2.

69. The method of any one of claims 1, 7, 36, 53, 54, and 55, wherein the EphA2 polypeptide is a chimeric polypeptide comprising at least an antigenic portion of EphA2 and a second polypeptide.

70. The method of claim 52 or 56, wherein the EphA2 antibody immunospecifically binds
5 to an epitope in the extracellular domain of EphA2.

71. The method of claim 52 or 56, wherein the EphA2 antibody immunospecifically binds to an epitope the intracellular domain of EphA2.

72. The method of any one of claims 1, 7, 36, 53, 54, and 55, wherein the EphA2 polypeptide is a chimeric polypeptide comprising at least an antigenic portion of EphA2 and
10 a second polypeptide.

73. The method of claim 1, or 53, wherein the composition comprises a plurality of EphA2 antigenic peptides.

74. The method of claim 7 or 54, wherein the composition comprises a plurality of EphA2 antigenic peptide expression vehicles.

15 75. The method of claim 7 or 54, wherein the expression vehicle expresses a plurality of EphA2 antigenic peptides.

76. The method of claim 36 or 55, wherein the antigen presenting cells are sensitized with a plurality of EphA2 antigenic peptides

20 77. The method of any one of claims 1, 7, 36, 52, 53, 54, 55, and 56, further comprising administering an additional anti-cancer therapy.

78. The method of claim 77, wherein the additional anti-cancer therapy is an agonistic EphA2 antibody.

79. The method of claim 77, wherein the additional anti-cancer therapy is chemotherapy, biological therapy, immunotherapy, radiation therapy, hormonal therapy, or surgery.

80. The method of any one of claims 1, 7, 36, 52, 53, 54, 55, and 56, wherein said administering is mucosal, intranasal, parenteral, intramuscular, intravenous, oral or intraperitoneal.

81. The method of any one of claims 1, 7, 36, 52, 53, 54, 55, and 56, wherein the administration elicits a CD4⁺ T-cell response, a CD8⁺ T-cell response, an innate immune response, an antibody response, or a combination of one or more of the foregoing.

82. The method of claim 81, wherein the administration elicits both a CD4⁺ T-cell response and a CD8⁺ T-cell response.

83. The method of claim 1, 7, 36 or 54, wherein the subject has a disease involving aberrant angiogenesis.

84. The method of claim 83, wherein the disease is macular degeneration, diabetic retinopathy, retinopathy of prematurity, vascular restenosis, infantile hemangioma, verruca vulgaris, psoriasis, Kaposi's sarcoma, neurofibromatosis, recessive dystrophic epidermolysis bullosa, rheumatoid arthritis, ankylosing spondylitis, systemic lupus, psoriatic arthropathy, Reiter's syndrome, and Sjogren's syndrome, endometriosis, preeclampsia, atherosclerosis or coronary artery disease.

85. A method of treating a human individual having a disease involving aberrant angiogenesis, said method comprising administering to the individual a composition comprising an EphA2 antigenic peptide in an amount effective to treat a disease involving aberrant angiogenesis.

86. A method of treating a human individual having a disease involving aberrant angiogenesis, said method comprising administering to the individual a composition comprising an EphA2 expression vehicle in an amount effective to treat a disease involving aberrant angiogenesis.

87. A method of treating a human individual having a disease involving aberrant angiogenesis, said method comprising administering to the individual a composition

comprising antigen presenting cells sensitized with an EphA2 antigenic peptide in an amount effective to treat a disease involving aberrant angiogenesis.

88. A method of treating a human individual having a disease involving aberrant angiogenesis, said method comprising administering to an individual a composition comprising an anti-idiotypic antibody or antigen-binding fragment thereof which immunospecifically binds to an idiotype of an anti-EphA2 antibody in an amount effective to elicit treat a disease involving aberrant angiogenesis.

89. The method of claim 85, 86, 87, or 88, wherein the disease is macular degeneration, diabetic retinopathy, retinopathy of prematurity, vascular restenosis, infantile hemangioma, verruca vulgaris, psoriasis, Kaposi's sarcoma, neurofibromatosis, recessive dystrophic epidermolysis bullosa, rheumatoid arthritis, ankylosing spondylitis, systemic lupus, psoriatic arthropathy, Reiter's syndrome, and Sjogren's syndrome, endometriosis, preeclampsia, atherosclerosis or coronary artery disease.

90. A method of producing antibodies that immunospecifically bind to EphA2 comprising administering an EphA2 vaccine to a host.

91. A method of treating a human individual having a hyperproliferative disorder of EphA2-expressing cells, said method comprising administering to the individual a composition comprising antibodies produced by administering an EphA2 vaccine to a host in an amount effective to treat a hyperproliferative disorder of EphA2-expressing cells.

92. A method of treating a human individual having a hyperproliferative disorder of EphA2-expressing cells, said method comprising (1) administering to the individual a composition comprising an EphA2 expression vehicle, selected from the group consisting of a bacterium or virus, in an amount effective to treat a hyperproliferative disorder of EphA2-expressing cells; and (2) administering to the individual an antibiotic or antiviral agent in an amount effective to treat a bacterial or viral infection.